Remarks/Arguments

Claims 1-3 and 52-54, as amended, appear in this application for the Examiner's review and consideration. Claims 42-50 have been canceled without prejudice. Applicants expressly reserve the right to pursue the subject matter of these claims in a divisional, continuation, or continuation-in-part application.

The specification has been amended to correct an inadvertent typographical error in the priority claim. The priority claim to U.S. provisional application Serial No. 60/261,051 has been corrected to read 60/261,052. The correct serial number of 60/261,052 is supported by the Declaration executed on March 10, 2002 (attached hereto as "Attachment A" for the Examiner's convenience), which recites that the application claims the benefit of U.S. provisional application Serial No. 60/261,052. Thus, the correction of this typographical error in the priority claim adds no new matter to the application. Once this amendment to the specification has been entered, Applicants respectfully request that the Office issue a filing receipt that has been updated to correct the priority claim to recite U.S. provisional application Serial No. 60/261,052, filed on January 11, 2001.

Claims 1-3 have been amended for clarity and to present the claims in better form. The units "by weight" have been added. This amendment is supported on page 3, line 27 of the application as filed. In addition, the term "exo-methylene" has been replaced with "exo-methylene by-product." This amendment is supported on page 3, lines 22-23 of the application as filed.

New claims 52-54 have been added. Claims 52-54 recite pharmaceutical formulations comprising the ondansetron of claims 1-3, respectively. These claims are supported by and replace original claims 45-47. One of skill in the art recognizes that a "pharmaceutical formulation" refers to a composition comprising an active pharmaceutical ingredient in a therapeutically effective amount and at least one pharmaceutically acceptable excipient.

Applicants appreciate the courtesies extended to their representatives, Craig L. Puckett, Reg. No. 43,023, and Gina R. Gencarelli, Reg. No. 59,729, during the interview with Examiner Laura Stockton conducted on February 20, 2007. The substance of the interview and the reasons presented at the interview as warranting favorable action are included in the comments below. As discussed in the interview, Applicants may submit an additional Rule 132 declaration in support of the patentability of the claims, if necessary.

Claims 45-47 and 50 were objected to under 37 C.F.R. § 1.75 as being substantial duplicates of claims 42-44 and 48, respectively. Office Action, pp. 5-6. This objection has been rendered moot by the cancellation of claims 42-50.

Claims 1-3 and 42-50 stand rejected under 35 U.S.C. § 103(a) as allegedly rendered obvious by Zhongguo Yiyao Gongye Zazhi 24, 241-242 (1993) ("the Zhongguo reference"), U.S. patent Nos. 4,845,115 to Tyers *et al.*, ("'115 patent"), 4,695,578 to Coates *et al.*, ("the '578 patent"), 4,835,173 to Tyers ("'173 patent"), and PCT publication WO 02/36558 ("WO '558") for the reasons set forth on pages 6-9 of the Office Action. This rejection has been rendered moot as to claims 42-50 by the cancellation of the claims. As to the remaining claims, Applicants respectfully traverse.

The cornerstone of the Office's § 103 rejection is the proposition that claims to pure forms of known compounds are *per se* obvious because "[c]hanging the form, purity, color, or other characteristic of an old product without a new use as a result thereof does not render [sic] product patentable where utility remains the same," citing *Ex parte Hartop*, 139 U.S.P.Q. 525 (Bd. Pat. App. & Interf. 1962). Office Action, p. 8. The Federal Circuit, its predecessor Court of Customs and Patent Appeals, and the Board of Patent Appeals and Interferences, however, have repeatedly denounced this type of *per se* analysis.

Recently in 2003, in an unpublished decision, the Board reversed an examiner's rejection of a new polymorphic form of a compound as *per se* obvious in view of the known compound, holding that *per se* rules of obviousness were improper and also substantially discredited the reasoning of *Hartop*. *See Ex parte Andrews*, Appeal No. 2002-0941, 2003 WL 25277872 (Bd. Pat. App. & Interf. September 25, 2003) (attached hereto as "Attachment B"). Importantly, the Board noted that it was improper for the examiner to rely on *Hartop* because the principle of law enunciated in *Hartop* had been "substantially discredited" in *In re Cofer*, 354 F.2d 664, 667-68 (C.C.P.A. 1966). *Id.* In *Andrews*, the examiner had based the obviousness rejection of the new polymorphic form on the prior art disclosure of the compound coupled with the *Hartop* reasoning (that a mere change in form is not enough to accord patentability to an otherwise known compound). *Id.* The Board reversed this rejection, holding that "reliance on **per se rules of obviousness is legally incorrect and must cease**." *Id.* (emphasis added) The Board found that the examiner did not make a *prima facie* case of obviousness because he failed to adequately explain how a person having ordinary skill would have been led from the prior art compound to the claimed polymorph. *Id.*

In *In re Cofer*, the Court of Customs and Patent Appeals reversed the Office's rejection of claims to a crystalline diepoxide compound as *per se* obvious in view of the disclosure of the compound as a viscous liquid. As in *Andrews*, the Office had based its obviousness rejection on the prior art disclosure of the compound coupled with the Board's reasoning in *Hartop*. The court discredited the Office's reliance on *Hartop*, concluding that the Board in *Hartop* had erred in its analysis. In particular, the court stated that in its decision in *Hartop* the Board "fail[ed] to support the broad proposition that 'merely changing the form, purity or other characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable.'" *In re Cofer*, 354 F.2d at 667. The court explained that the legal conclusion of obviousness must be based upon facts appearing in the record, rather than *per se* rules, and that factors to be considered included "whether the prior art suggest[ed] the particular structure or form of the compound or composition as well as suitable methods of obtaining that structure of form." *Id.* at 667-68. Since then the C.C.P.A., the Federal Circuit, and the Board have followed this analysis.

Following *Cofer*, again the Court of Customs and Patent Appeals in *In re Hoeksema*, 399 F.2d 269 (C.C.P.A. 1968), reversed the Office's rejection of an N-psicofuranoside as obvious in view of the prior art disclosure of a structurally similar homolog of the compound, concluding that "if the prior art of record fails to disclose or render obvious a method for making a claimed compound, at the time the invention was made, it may not be legally concluded that the compound itself is in possession of the public" and, thus, "the absence of a known or obvious process for making the claimed compounds overcomes a presumption that the compounds are obvious, based on close relationships between their structures and those of the prior art compounds." *Id.* at 274. The Federal Circuit reiterated this position more recently in *In re Kumar*, 418 F.3d 1361 (Fed. Cir. 2005), reversing the Office's rejection of claims directed to aluminum oxide particles having a particular particle size distribution as obvious in view of a prior art disclosure of aluminum oxide particles. The reference was silent as to the particle size distribution. The Federal Circuit reversed the Office's obviousness rejection in part because the Office had not established that the prior art would have enabled one of skill in the art to produce aluminum oxide particles with the claimed particle size distribution.

Over the past decade, the Board has repeatedly reversed § 103 rejections of claims to new polymorphic forms of known compounds, applying the principles established by the Court of Customs and Patent Appeals in *Cofer* and *Hoeksema*. For example, in *Ex parte*

Gala, Appeal No. 2001-0987, 2002 WL 851814, *3 (Bd. Pat. App. & Interf.) (attached hereto as "Attachment C"), the Board reversed an examiner's rejection of claims to loratadine polymorphic form 2 as *per se* obvious over the prior art disclosure of loratadine polymorphic form 1. Unconvinced by the examiner's reasoning, the Court held that the rejection was improper because "the examiner...has not adequately established that the prior art (1) suggests the polymorph form 2 of loratadine; or (2) discloses or renders obvious a method for making the polymorph form 2 of loratadine." *See Gala*, 2002 WL at *3. The Board has continued to follow the reasoning set forth in *Gala* in several unpublished decisions.[1]

It is clear from the above-described case law that to render claims to new forms of prior art compounds obvious, the prior art must disclose or suggest that the compound may assume the new form and a process for making the claimed form.

Claims 1-3 of the instant application recite a new form of the known compound ondansetron hydrochloride dihydrate – "Ondansetron hydrochloride dihydrate having a purity of at least about 99.0% by weight and an exo-methylene by-product content of less than 0.01% by weight."

As previously argued, the cited art does not disclose or suggest either explicitly or inherently the purity of the compound recited in the claims. *See, e.g.*, Amendment dated August 14, 2006, pp. 7-8. Further, none of the cited references, either alone or in combination, teaches or suggests a suitable method for obtaining ondansetron hydrochloride dihydrate of the purity recited in the claims. *In re Hoeksema, supra.*

Applicants made ondansetron hydrochloride dihydrate having less than 0.01% by weight of exo-methylene by-product from ondansetron base using a two-prong approach: (i) minimizing the amount of exo-methylene by-product present in the starting ondansetron base and (ii) purifying the ondansetron hydrochloride dihydrate to remove any remaining exo-methylene by-product.

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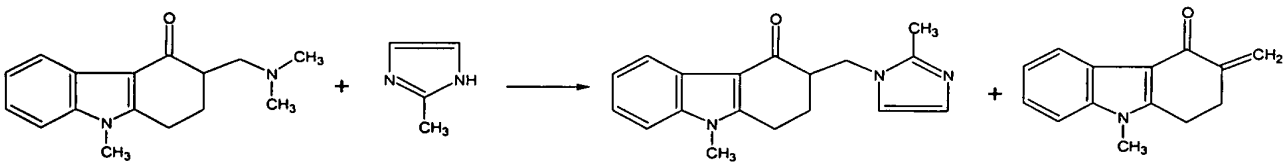
[1] *See also Ex parte Havens*, Appeal No. 2001-0091, 2003 WL 21279863 (Bd. Pat. App. & Interf.) (reversing a § 103 rejection of claims to delaviridine mesylate in the S and T crystal forms in view of the prior disclosure of delvaridine mesylate itself because the examiner had "provided no evidence or convincing reasoning why the prior art disclosure of delavirdine mesylate in an undefined state would have suggested the specific S and T crystal forms that are the subject of the instant claims"); *Ex parte Meisel*, Appeal No. 2002-0438, 2002 WL 32334598 (Bd. Pat. App. & Interf. October 10, 2002) (reversing a rejection of claims to polymorphs of a known compound as obvious in view of the prior art disclosure of the compound itself because the prior art did not teach or suggest that the compound had different crystalline structures); *Ex parte Polniaszek*, Appeal No. 2001-1805, 2003 WL 22282265 (Bd. Pat. App. & Interf.) (reversing a similar rejection of claims to polymorphic forms of a known compound and stating that "we wish to make it clear that 'reliance on per se rules of obviousness is legally incorrect'"). These three unpublished decisions are attached hereto as "Attachment D" for the Examiner's convenience.

The exo-methylene by-product is one of the main impurities produced when ondansetron base is synthesized from dimethylamino-methyl-carbazolone and methyl-imidazole, as illustrated below.



dimethylamino-methyl-carbazolone methyl-imidazole ondansetron base exo-methylene by-product

Specification, p. 1, l. 34 to p. 2, l. 2. Applicants have found that the amount of exo-methylene by-product produced is inversely related to the amount of methyl-imidazole starting material used. *See* Rule 132 Declaration of Dr. Lidor-Hadas ("Lidor-Hadas Declaration"), p. 2, ¶ 5 and Table 1. Thus, by controlling the amount of methyl-imidazole, Applicants have been able to limit the production of the exo-methylene by-product. Further, Applicants have found that the remaining exo-methylene by-product content of the ondansetron base can be further reduced by crystallization in the presence of activated carbon. Specification, p. 7, ll. 13-15; *see also* Lidor-Hadas Declaration, Table 1. The purified ondansetron base, thus obtained, is then converted into ondansetron hydrochloride dihydrate, which is further purified by crystallization from water in the presence of activated carbon to reduce the exo-methylene by-product content to less than 0.01%. Specification, p. 7, ll. 25-29; p. 10, ll. 23-32. None of the cited references either teaches or suggests a method that can obtain ondansetron hydrochloride dihydrate with this level of purity.

The Zhongguo reference discloses the synthesis of ondansetron base by the reaction of dimethylamino-methyl-carbazolone with 2.7 equivalents of methyl-imidazole, followed by crystallization from methanol. Zhongguo reference, p. 2 (example 3). The Zhongguo reference further discloses the preparation of ondansetron hydrochloride dihydrate from the ondansetron base. *Id.* The ondansetron hydrochloride dihydrate thus obtained is isolated by extraction. *Id.* The Zhongguo reference does not teach or suggest any method for further purifying the ondansetron hydrochloride dihydrate.

The Lidor-Hadas Declaration establishes that when 3 equivalents of methyl-imidazole are used, the ondansetron base produced has an exo-methylene by-product content of 7.3%. *See* Lidor-Hadas Declaration, p. 2, Table 1, reproduced below. The Lidor-Hadas Declaration

also establishes that this exo-methylene by-product content can be reduced to 1.47% by crystallization. *Id.*

TABLE 1

REFERENCE		EB-308		OZ-371		AD-283	
MI EQUIVALENTS		3		4		5	
OND BASE		CRUDE	CRYST	CRUDE	CRYST	CRUDE	CRYST
HPLC AREA %	EXO-METHYLENE	7.3	1.47	5.6	0.96	4.8	0.74
	OND BASE	90.0	98.1	91.7	98.3	92.9	98.6
	DMA-Me-CAR	1.40	0.23	1.80	0.40	1.60	0.40

Id (emphasis added).

Therefore, at best, the Zhongguo reference discloses the production of ondansetron base having 1.47% exo-methylene by-product. The exo-methylene content of the ondansetron base is carried over to the ondansetron hydrochloride dihydrate, as illustrated by Table 2 of the Lidor-Hadas Declaration, reproduced below.

TABLE 2

PURIFICATION OF OND.HCl.$2H_2O$ FROM exo-METHYLENE BY-PRODUCT WITH SX-1 CARBO

ENTRY	REFERENCE OZ-	% SX-1 CARBO	AREA % OF EXO-METHYLENE (HPLC)			
			OND BASE	OND.HCl.$2H_2O$ CRUDE	OND.HCl.$2H_2O$ PURE	
					FIRST CRYSTAL.	SECOND CRYSTAL.
1	442	5	0.88	0.70	-	0.05
2	451	5	0.90	0.68	-	0.01
3	441	5	1.40	0.93	-	0.06
4	452	5	1.30	1.30	-	0.05
5	444	5	1.74	1.43	-	0.20
6	453	5	1.68	1.67	-	0.14
7	456-A	5	-	2.40	1.30	0.54
8	456-B	10	-	2.40	0.70	0.16
9	456-C	15	-	2.40	0.42	0.05
10	455	5	0.95	1.02	-	0.19
11	457	5	0.85	0.35*	-	0.01

*OND.HCl2H_2O crude was prepared with 5% SX-1.

Lidor-Hadas Declaration, p. 5, Table 2 (emphasis added).

Because the Zhongguo reference does not disclose any method for purifying the ondansetron hydrochloride dihydrate, it cannot disclose or render obvious a method that can reduce the exo-methylene content from approximately 1.47% to less than 0.01%, *i.e.*, accomplish a 147-fold increase in purity, as recited in the claims.

The '578, '173, and '115 patents (collectively "the Glaxo patents") disclose the synthesis of ondansetron base by the reaction of dimethylamino-methyl-carbazolone with 3 equivalents of methyl-imidazole, followed by crystallization from methanol. '578 patent, col. 19, ll. 42-55 (example 7); '115 patent, col. 3, ll. 40-52 (example 1); '173 patent, col. 3, ll. 31-43 (example 1). The Glaxo patents further disclose the conversion of the ondansetron base to ondansetron hydrochloride dihydrate, followed by crystallization from a mixture of isopropanol and water. '578 patent, col. 20, ll. 27-47 (example 10); '115 patent, col. 3, l. 53 to col. 4, l. 4 (example 2); '173 patent, col. 3, ll. 44-64 (example 2). The Lidor-Hadas Declaration establishes that this process yields ondansetron hydrochloride dihydrate having an exo-methylene by-product content of 0.12%. *See* Lidor-Hadas Declaration, p. 1, ¶ 3, p. 4. None of the Glaxo patents teaches or suggests a method for reducing the exo-methylene by-product content 12-fold, *i.e.*, from 0.12% to less than 0.01%, as recited in the claims.

The Office asserts that the recrystallization step of the Glaxo patents renders obvious the ondansetron hydrochloride dihydrate of the purity recited in the claims:

> Since recrystallization is a known process for purifying a compound, one skilled in the art would expect the obtained product to be of a high purity.

Office Action, p. 10 (internal citations omitted).

Applicants respectfully point out that recrystallization does not necessarily yield a product of high purity, as the Office suggests. There are many factors that affect the purity of a product obtained by crystallization, including, for example, choice of solvent, concentration, or temperature at which the crystallization is performed. Further, even assuming *arguendo* that each recrystallization can produce a linear increase in purity, to achieve the purity recited in the claims the skilled artisan would have to perform many more recrystallizations of the product of the Glaxo patents to reduce the exo-methylene by-product content from 0.12% to less than 0.01%.

The Lidor-Hadas Declaration establishes that the crystallization process disclosed in the Glaxo patents reduces the exo-methylene by-product content from 0.4% to 0.12%, which corresponds to a 30% increase in purity. Assuming a linear increase in purity, the

crystallization process of the Glaxo patents would have to be repeated three more times to reduce the exo-methylene by-product content from 0.12% to less than 0.01%. Because each crystallization results in loss of product, such a process would be unsuitable to produce the recited ondansetron hydrochloride dihydrate in any substantial amount (three crystallizations, each increasing the purity by 30%, would result in a 90% loss in product yield). By their choice of solvent and use of activated carbon during crystallization, Applicants have been able to reduce the exo-methylene by-product content to less than 0.01% from levels as high as 0.68% in two crystallizations. *See* Lidor-Hadas Declaration, p. 5, Table 2 (entry 2).

WO '558 discloses a method for converting ondansetron base into ondansetron hydrochloride dihydrate by treating a solution of ondansetron base in a mixture of ethanol and isopropanol with hydrochloric acid. WO '558, p. 16, ll. 20-25 (example 3). The ondansetron hydrochloride dihydrate is then isolated by evaporating the solvent. *Id.* WO '558 does not disclose a method for preparing the ondansetron base and does not disclose the presence of the exo-methylene by-product. Further, WO '558 does not disclose any method for purifying the ondansetron hydrochloride dihydrate at all, let alone a method that can produce ondansetron hydrochloride dihydrate with an exo-methylene by-product content of less than 0.01%, as recited in the claims.

The combination of references at least requires selective picking and choosing of crystallization conditions (if mentioned) to obtain the compound of the recited purity. The Zhongguo reference and WO '558 do not disclose the crystallization of ondansetron hydrochloride dihydrate at all. Thus, in choosing to purify the ondansetron hydrochloride dihydrate by crystallization, the skilled artisan would have to ignore the teachings of these references. Further, as to the Glaxo patents, the skilled artisan would have to choose to remove the crystallization solvent isopropanol and choose to add activated carbon in order to crystallize ondansetron hydrochloride dihydrate of the recited purity. The Office does not point to any guidance among the many references for any such combination.

Thus, because the cited references, either alone or in combination, do not teach or suggest ondansetron hydrochloride dihydrate of the recited purity or a suitable process for obtaining ondansetron hydrochloride dihydrate of the recited purity, the cited references cannot render the claims obvious. *In re Hoeksema, supra.* Accordingly, the rejection of claims 1-3 and 42-50 under 35 U.S.C. § 103(a) as rendered obvious by the Zhongguo reference, the '115 patent, the '578 patent, the '173 patent, and the WO '558 publication cannot stand and should be withdrawn.

Finally, Applicants note that the Office dismisses the Federal Circuit and Court of Customs and Patent Appeals decisions of *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995) (holding that in the case of new chemical compounds, until they are actually isolated and purified, it would be highly unlikely for one of ordinary skill in the art to contemplate what was ultimately obtained; what cannot be contemplated or conceived cannot be obvious), *In re Seaborg*, 382 F.2d 996 (C.C.P.A. 1964) (holding that a prior art reference must enable one of skill in the art to practice the claimed invention in order to render the claims invalid), and *In re Bergstrom*, 427 F.2d 1394 (C.C.P.A. 1970) (holding that pure materials may be patentable over less pure or impure materials), by distinguishing their facts from those of the instant application, while ignoring the overriding principles of law. Office Action, pp. 11-12. Although the facts of this application may be different from those of the cited cases, the principles of law are equally applicable to this application.

In view of the foregoing arguments, it is believed that claims 1-3 and 52-54 are now in condition for allowance, early notice of which would be appreciated. If any outstanding issues remain, the Examiner is invited to telephone the undersigned at the telephone number indicated below to discuss the same. No fee is believed to be due for the submission of this response. Should any fees be required, please charge such fees to Kenyon & Kenyon, LLP Deposit Account No. 11-0600.

Respectfully submitted,

Dated: May 2, 2007

By: Gina R Gencarelli
Gina R. Gencarelli
Reg. No. 59,729

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CUSTOMER NUMBER 26646

ATTACHMENT A

U.S. DEPARTMENT OF COMMERCE
PATENT AND TRADEMARK OFFICE

DECLARATION

ATTORNEY'S DOCKET NO.
1662/55602

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled **A NOVEL PROCESS FOR PREPARING PURE ONDANSETRON HYDROCHLORIDE DIHYDRATE,** the specification of which was filed on January 11, 2002 as U.S. Serial No. 10/045,970.

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations, § 1.56.

PRIOR UNITED STATES APPLICATION(S)

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below.

APPLICATION NUMBER	FILING DATE (day, month, year)
60/261,052	11 January 2001

SEND CORRESPONDENCE, AND DIRECT TELEPHONE CALLS TO:

Steven J. Lee

26646
PATENT TRADEMARK OFFICE

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under § 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

FULL NAME OF INVENTOR	FAMILY NAME LIDOR-HADAS	FIRST GIVEN NAME Rami	SECOND GIVEN NAME
RESIDENCE & CITIZENSHIP	CITY Kfar Saba 44242	STATE OR FOREIGN COUNTRY Israel	COUNTRY OF CITIZENSHIP Israel
POST OFFICE ADDRESS	POST OFFICE ADDRESS 19 Mor Street	CITY Kfar Saba 44242	STATE & ZIP CODE/COUNTRY Israel
Signature		Date 10.3.02	

FULL NAME OF INVENTOR	FAMILY NAME BACHAR	FIRST GIVEN NAME Eliezer	SECOND GIVEN NAME
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POST OFFICE ADDRESS	POST OFFICE ADDRESS 95 Haim Levanon Street	CITY Tel Aviv 69345	STATE & ZIP CODE/COUNTRY Israel
Signature		Date 10.3.2002	

FULL NAME OF INVENTOR	FAMILY NAME	FIRST GIVEN NAME	SECOND GIVEN NAME
RESIDENCE & CITIZENSHIP	CITY	STATE OR FOREIGN COUNTRY	COUNTRY OF CITIZENSHIP
POST OFFICE ADDRESS	POST OFFICE ADDRESS	CITY	STATE & ZIP CODE/COUNTRY
Signature		Date	

ATTACHMENT B

2003 WL 25277872 (Bd.Pat.App & Interf.)
(Cite as: 2003 WL 25277872 (Bd.Pat.App & Interf.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)
EX PARTE DAVID R. ANDREWS, WILLIAM LEONG, AND ANANTHA SUDHAKAR
Appeal No. 2002-0941
Application No. 09/166,445
September 25, 2003

Before WINTERS, SCHEINER, and GRIMES

Administrative Patent Judges

WINTERS

Administrative Patent Judge

ON BRIEF

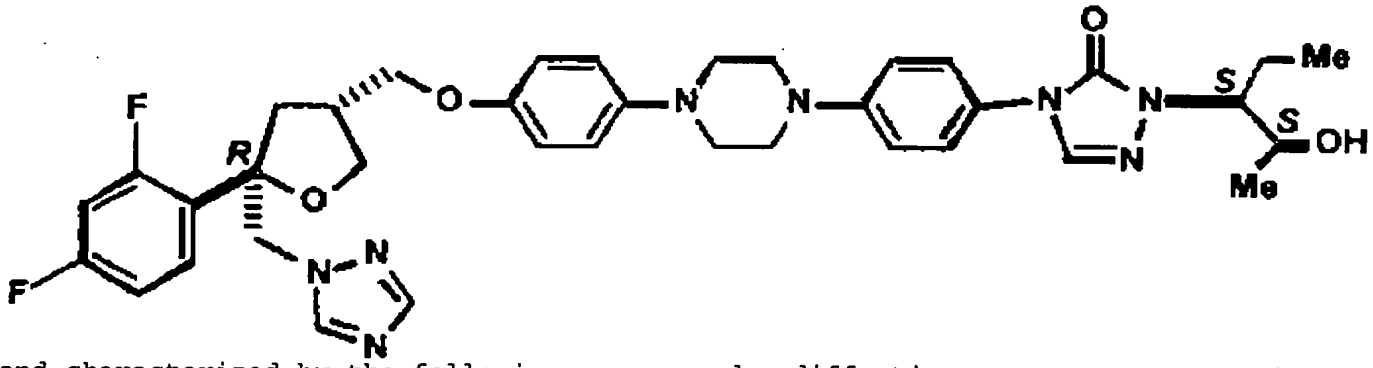
DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 1 through 5, which are all the claims pending in the application.

The Invention

Applicants have discovered that the compound having formula I can exist in the form of three crystalline **polymorphs**, each distinctly different from each other and from the amorphous form in physico-chemical data, physical properties, and methods of preparation. These crystalline **polymorphs** are referred to as Form I, Form II, and Form III (specification, page 2, second paragraph). Form I, said to be the most stable of these forms, is the subject of representative claim 1 which reads as follows:

(1) A crystalline **polymorph** form of 1 of(-)-4-[4-[4-[4-[[(2R-cis)-5-(2,4-difluorophenyl)tetrahydro- 5-(1H-2,4-triazol-1-ylmethyl)furan-3-yl]-methoxy]phenyl]-1-piperazinyl] phenyl-2,4-dihydro-2-[(S)-1-ethyl-2(S)-hydroxylpropyl]-3H-1,2,4,-triazol-3-one represented by formula I



and characterized by the following x-ray powder diffaction pattern expressed in

terms of "d" spacing and relative intensities ("RI"):

d spacing (+-0.04)	R1
6.10	Medium
4.63	Medium
4.10	Wide
3.69	Wide
3.05	Wide

The Prior Art Reference

In rejecting applicants' claims under 35 U.S.C. § 102(e) and 35 U.S.C. § 103(a), the examiner relies on the following reference:

Andrews et al. (Andrews) 5,625,064 Apr. 29, 1997

The Rejections

The appealed claims stand rejected as follows:

(1) claims 1, 2, and 3 under 35 U.S.C. § 112, second paragraph, as indefinite;

(2) claims 1 through 5 under 35 U.S.C. § 102(e) as anticipated by Andrews; and

(3) claims 1 through 5 under 35 U.S.C. § 103(a) as unpatentable over Andrews.

Deliberations

Our deliberations in this matter have included evaluation and review of the following materials:

*2 (1) the instant specification, including all of the claims on appeal;

(2) applicants' Appeal Brief (Paper No. 17);

(3) the Examiner's Answer (Paper No. 18); and

(4) the above-cited prior art reference.

On consideration of the record, including the above-listed materials, we reverse each of the examiner's rejections.

Section 112

In our judgment, claims 1, 2, and 3 set out and circumscribe a particular area with a reasonable degree of precision and particularity; and the examiner's rejection of these claims under 35 U.S.C. § 112, second paragraph, for indefiniteness, lacks merit. We shall not belabor the record with extensive commentary on this point, but simply refer to applicants' discussion in the Appeal Brief, pages 3 and 4, with which we agree. Additionally, the examiner does not invite attention to any language or limitation in claims 1, 2, or 3 which would give rise to a case of indefiniteness.

The rejection under 35 U.S.C. § 112, second paragraph, is reversed.

Section 102(e)

The examiner argues that (1) Andrews describes a compound having formula I illustrated in claim 1 on appeal; and (2) Andrews discloses that that compound possesses antifungal activity. With respect to the particular polymorphic form recited in the appealed claims (crystalline **polymorph** form I), the examiner acknowledges that "Andrews is silent to [sic] as to nature of crystalline form produced" (Paper No. 18, page 4, first full paragraph). Nevertheless, the examiner would shift the burden of persuasion to applicants to establish that the prior art compound disclosed by Andrews lacks the x-ray powder diffraction pattern and infrared spectrum characteristics recited in applicants' claims ("evidence in verified form is needed that the prior art compound inherently lacks the characteristics relied on" id.). This constitutes reversible error.

As stated in the specification, page 2, second paragraph, applicants have discovered that the compound of formula I can exist in the form of three crystalline **polymorphs**, each distinctly different from each other and from the amorphous form. These crystalline **polymorphs** are referred to in the specification as Form I, Form II, and Form III and, according to applicants, Form I is the most stable.

The examiner does not deny that applicants' specification teaches any person skilled in the art how to make crystalline **polymorph** form I of the compound of formula I illustrated in claim 1 on appeal. Nor can the examiner point to any passage in Andrews disclosing applicants' method for making crystalline **polymorph** form I, or establishing a reasonable basis for concluding that the prior art compound disclosed by Andrews meets all the limitations of the claims. On the contrary, the examiner acknowledges that "Andrews is silent to [sic] as to nature of crystalline form produced" (Paper No. 18, page 4, first full paragraph).

***3** On these facts, the examiner is not in a position to invoke the principles enunciated in In re Fitzgerald, 619 F.2d 67, 70, 205 USPQ 594, 596-97 (CCPA 1980); In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433-34 (CCPA 1977); and In re Swinehart, 439 F.2d 210, 213, 169 USPQ 226, 229 (CCPA 1971). Rather, the facts here more closely resemble those presented to another merits panel of this board in Ex parte Skinner, 2 USPQ2d 1788 (Bd. Pat. App. & Int. 1986). As stated by the board in Skinner:

> We are mindful that there is a line of cases represented by In re Swinehart, 439 F.2d 210, 169 USPQ 226 (CCPA 1971) which indicates that where an examiner has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, the examiner possesses the authority to require an applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. Nevertheless, before an applicant can be put to this burdensome task, the examiner must provide some evidence or scientific reasoning to establish the reasonableness of the examiner's belief that the functional limitation is an inherent characteristic of the prior art. In the case before us, no such evidence or reasoning has been set forward. [id. at 1789]

The rejection under 35 U.S.C. § 102(e) is reversed.

Section 103(a)

Citing Ex parte Hartop, 139 USPQ 525 (Bd. App. 1962), the examiner apparently would invoke a per se rule of obviousness, viz., that merely changing the form, purity, or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable. The examiner argues that (1) crystalline **polymorph** form I of the compound of formula I

illustrated in claim 1 on appeal is merely a different polymorphic form of the compound disclosed by Andrews having formula I; (2) crystalline **polymorph** form I recited in applicants' claims and the compound disclosed by Andrews having formula I both possess antifungal activity; and (3) accordingly, the subject matter sought to be patented in claims 1 through 5 would have been prima facie obvious in view of Andrews. We disagree.

First, as stated in In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995):

> The use of per se rules, while undoubtedly less laborious than a searching comparison of the claimed invention--including all its limitations--with the teachings of the prior art, flouts section 103 and the fundamental case law applying it. Per se rules that eliminate the need for fact-specific analysis of claims and prior art may be administratively convenient for PTO examiners and the Board. Indeed, they have been sanctioned by the Board as well. But reliance on per se rules of obviousness is legally incorrect and must cease.

***4** Second, the principle of law enunciated in Ex parte Hartop, 139 USPQ 525 (Bd. App. 1962) has been substantially discredited in In re Cofer, 354 F.2d 664, 667-<c><c>68, 148 USPQ 268, 270-71 (CCPA 1966).

Third, on this record, the examiner has not adequately explained how a person having ordinary skill would have been led from "here to there," i.e., from the Andrews compound having formula I to the crystalline **polymorph** form I recited in claims 1 through 5.

The rejection under 35 U.S.C. § 103(a) is reversed.

Conclusion

In conclusion, for the reasons set forth, we do not sustain the rejection of claims 1, 2, and 3 under 35 U.S.C. § 112, second paragraph; the rejection of claims 1 through 5 under 35 U.S.C. § 102(e); or the rejection of claims 1 through 5 under 35 U.S.C. § 103(a).

The examiner's decision rejecting claims 1 through 5 is reversed.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

Sherman D. Winters

Administrative Patent Judge

Toni R. Scheiner

Administrative Patent Judge

Eric Grimes

Administrative Patent Judge

Schering-Plough Corporation

Patent Department (K-6-1, 1990)

2000 Galloping Hill Road

Kenilworth, NJ 07033-0530

2003 WL 25277872 (Bd.Pat.App & Interf.)

END OF DOCUMENT

ATTACHMENT C

2002 WL 851814 (Bd.Pat.App & Interf.)
(Cite as: 2002 WL 851814 (Bd.Pat.App & Interf.))

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)
*1 EX PARTE DINESH GALA AND DONALD J. DIBENEDETTO
Appeal No. 2001-0987
Application 09/169,109

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

Thomas D. Hoffman

Schering-Plough Corporation

Patent Department K-6-1 1990

2000 Galloping Hill Road

Kenilworth NJ 07033-0530

Before WINTERS, WILLIAM F. SMITH, and ROBINSON

Administrative Patent Judges

Winters

Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

This appeal was taken from the examiner's decision rejecting claims 1 through 8, which are all of the claims pending in this application.

THE INVENTION

Applicants' invention relates to a crystalline "polymorph form 2 loratadine" having a specified x-ray powder diffraction pattern; a pharmaceutical composition comprising an anti-allergic effective amount of the polymorph form 2 loratadine and a pharmaceutically acceptable carrier; and a method of treating allergic reactions in a mammal by administering to the mammal an anti-allergic effective amount of polymorph form 2 loratadine. Claim 1, which is illustrative of the subject matter on appeal, reads as follows:

1. Polymorph form 2 loratadine having the following x-ray powder diffraction pattern expressed in terms of "d" spacing and relative intensities("RI").

d spacing (+-0.05)	RI
8.95	Weak
6.37	Weak
5.64	Weak

THE REFERENCES

The prior art references relied on by the examiner are:

Villani	4,282,233	Aug. 4, 1981
Sims et al. (Sims) (PCT Application)	WO 95/01792	Jan.19, 1995

THE REJECTIONS

Claims 1 through 8 stand rejected under 35 U.S.C. § 103(a) as unpatentable over the combined disclosures of Villani and Sims. Claims 1 through 8 further stand rejected under the judicially created doctrine of obviousness-type double patenting over claim 7 of Villani in view of Sims.

DELIBERATIONS

Our deliberations in this matter have included evaluation and review of the following materials: (1) the instant specification, including Figures 1 and 2, and all of the claims on appeal; (2) the Appeal Brief (Paper No. 10); (3) the Examiner's Answer (Paper No. 11); and (4) the above - cited prior art references.

On consideration of the record, including the above - listed materials, we reverse the examiner's rejections.

DISCUSSION

The question here is whether the combined disclosures of Villani and Sims support a conclusion of obviousness of claims 1 through 8, which recite the crystalline polymorph form 2 of loratadine having a unique x-ray powder diffraction pattern and infrared spectrum. We answer that question in the negative.

*2 Villani discloses polymorph form 1 of loratadine, but does not disclose or suggest that loratadine may assume distinct, crystalline polymorphic forms having different physical properties. Nor does Villani teach a person having ordinary skill in the art how to make polymorph form 2 of loratadine.

The Sims reference does not cure the deficiencies of Villani. Sims discloses a list of 16 non-sedating antihistamines, including loratadine, useful in combination therapy (Sims, page 8, lines 3 through 6). After listing those antihistamines, Sims refers to "a pharmaceutically acceptable salt, hydrate, or polymorph thereof" (id., lines 6 and 7). That reference to pharmaceutically acceptable salts, hydrates, or polymorphs, however, does not teach a person having ordinary skill in the art that loratadine may assume distinct, crystalline polymorphic forms having different physical properties. Rather, it appears that the above-quoted language constitutes boilerplate; and that Sims refers generally to pharmaceutically acceptable salts, hydrates, or polymorphs of any one of 16 non-sedating antihistamines without specifically suggesting that loratadine is capable of existing in the form of distinct crystalline polymorphs. On this point, we disagree with the examiner's finding that "Sims expressly teaches that loratadine may be in the form of polymorphs" (Examiner's Answer, page 3, lines 10 and 11). Nor does Sims teach a person having ordinary skill in the art how to make polymorph form 2 of loratadine.

On this record, applicants, and applicants alone, disclose that "loratadine can exist in the form of two distinct crystalline polymorphs, each having distinctly different physical properties" (Specification, page 2, first full paragraph). Applicants have discovered specific solvents and experimental conditions, producing a distinctly different polymorph form 2 of loratadine (Specification, page 3, last paragraph). Applicants discovered that crystallization of loratadine (prepared as described in U.S. Patent No. 4,282,233) from toluene, t-butylmethylether, heptane, or mixtures thereof, produce a polymorph form 2 loratadine. Applicants also discovered that using a t-butylmethylether-toluene mixture is preferred (Specification, page 4, second paragraph). This information stems from applicants' specification, but not from the cited prior art. Further, neither Villani nor Sims discloses or renders obvious a method for making polymorph form 2 loratadine. As stated in In re Hoeksema, 399 F.2d 269, 274, 158 USPQ 596, 601 (CCPA 1968),

> [I]f the prior art of record fails to disclose or render obvious a method for making a claimed compound, at the time the invention was made, it may not be legally concluded that the compound itself is in the possession of the public. In this context, we say that the absence of a known or obvious process for making the claimed compounds overcomes a presumption that the compounds are obvious, based on close relationships between their structures and those of prior art compounds. [footnote omitted]

***3** The examiner relies heavily on this proposition of law set forth in Ex parte Hartop, 139 USPQ 525, 527 (Bd. Pat. App. 1962):

> [M]erely changing the form, purity or another characteristic of an old product, the utility remaining the same as that for the old product, does not render the claimed product patentable.

According to the examiner, polymorph form 2 loratadine is merely another form of an old product (polymorph form 1 loratadine) and both forms possess the same utility. Accordingly, the examiner concludes that applicants' claims, reciting polymorph form 2 loratadine, are unpatentable. We disagree. Here, we invite attention to In re Cofer, 354 F.2d 664, 667, 148 USPQ 268, 271 (CCPA 1966), where the court substantially discredited PTO reliance on the above-quoted proposition of law in Hartop. Like the situation presented in Cofer, the examiner in this case has not adequately established that the prior art (1) suggests the polymorph form 2 of loratadine; or (2) discloses or renders obvious a method for making the polymorph form 2 of loratadine.

Accordingly, the examiner's rejection of claims 1 through 8 under 35 U.S.C. § 103(a) as unpatentable over Villani in view of Sims is reversed. For essentially the same reasons, the rejection of claims 1 through 8 under the judicially created doctrine of obviousness-type double patenting over claim 7 of Villani in view of Sims is also reversed.

The examiner's decision rejecting claims 1 through 8 is reversed.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

Sherman D. Winters

Administrative Patent Judge

William F. Smith

Administrative Patent Judge

Douglas W. Robinson

Administrative Patent Judge

2002 WL 851814 (Bd.Pat.App & Interf.)

END OF DOCUMENT

ATTACHMENT D

2003 WL 21279863 (Bd.Pat.App & Interf.)
(Cite as: 2003 WL 21279863 (Bd.Pat.App & Interf.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)
EX PARTE JEFFREY L. HAVENS, DONALD P. SMITH, MICHAEL S. BERGREN AND MARK A. LYSTER
Appeal No. 2001-0091
Application No. 08/732,254

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

BRUCE STEIN

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INTELLECTUAL PROPERTY LEGAL SERVICES

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Before WINTERS, ROBINSON, and GRIMES

Administrative Patent Judges

GRIMES

Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

An oral hearing in this case was scheduled for November 27, 2001. Upon reviewing the case, however, we have determined that an oral hearing will not be necessary and we render the following decision based on the record.

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1 and 2. Claims 1 and 2 are directed to specific crystal forms (form "S" and form "T," respectively) of 1-[5- Methanesulfonamidoindolyl-2-carbonyl]-4-[3-(1-methylethylamino)-2-pyridinyl]-piperazine. monomethanesulfonate salt. [FN1] The claims list the powder **X-ray diffraction** measurements that distinguish the claimed crystal forms from other forms of delavirdine mesylate.

The examiner relies on the following reference:

Palmer et al. (Palmer) 5,563,142 Oct. 8, 1996

Claims 1 and 2 stand rejected under 35 U.S.C. § 102(e) as anticipated by Palmer.

Claims 1 and 2 also stand rejected under 35 U.S.C. § 103 as obvious over Palmer.

Claims 1 and 2 also stand rejected for both statutory and obviousness-type double patenting, based on the claims of Palmer.

We reverse all of the rejections.

Discussion

The claims are directed to delavirdine mesylate in the S crystal form (claim 1) or in the T crystal form (claim 2). The examiner rejected the claims, under several different rationales, over the Palmer patent.

1. Statutory double patenting

The examiner rejected the claims under 35 U.S.C. § 101 "as claiming the same invention as that of claim 11 of prior U.S. Patent No. 5563142." Examiner's Answer, page 4. The examiner explained that "[i]n the absence of evidence showing otherwise, either of the instant claims may be the same compound recited in US'142." Id.

"35 U.S.C. § 101 prevents two patents from issuing on the same invention.... A good test, and probably the only objective test, for 'same invention,' is whether one of the claims could be literally infringed without literally infringing the other. If it could be, the claims do not define identically the same invention.... If it is determined that the same invention is being claimed twice, 35 U.S.C. § 101 forbids the grant of the second patent." In re Vogel, 422 F.2d 438, 441, 164 USPQ 619, 621-22 (CCPA 1970).

***2** Here, the patent's claim 11 is directed to delavirdine mesylate, without limitation as to crystal form. Instant claims 1 and 2 are directed to delavirdine mesylate in the S and T crystal forms, respectively. Thus, delavirdine mesylate in any crystal form other than S or T, or in a noncrystalline form, would infringe Palmer's claim 11 without infringing either of the claims on appeal. Therefore, the claims on appeal are not directed to the "same invention" as Palmer's claim 11 and are not unpatentable on that basis. The rejection under 35 U.S.C. § 101 is reversed.

2. Anticipation

The examiner rejected the claims under 35 U.S.C. § 102(e) on the basis that "Palmer discloses by name the same chemical compound as the mono methanesulfonate salt. See claim 11 in the US patent. In view of this fact evidence is needed that the prior art compound inherently lacks the characteristics (**x-ray diffraction** spectra recited in claims 1 and 2) relied on herein." Examiner's Answer, page 3.

"A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros., Inc. v. Union Oil Co., 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "An inherent structure, composition or function is not necessarily known.... Insufficient prior understanding of the inherent properties of a known composition does not defeat a finding of anticipation." Atlas Powder Co. v. IRECO Inc., 190 F.3d 1342, 1349, 51 USPQ2d 1943, 1947 (Fed. Cir. 1999).

"'Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient."' In re Oelrich, 666 F.2d 578, 581, 212 USPQ 323, 326 (CCPA 1981)

(quoting Hansgirg v. Kemmer, 102 F.2d 212, 214, 40 USPQ 665, 667 (CCPA 1939)). When the inherent properties of a prior art product are at issue, "the examiner must provide some evidence or scientific reasoning to establish the reasonableness of the examiner's belief that the functional limitation is an inherent characteristic of the prior art" before the burden is shifted to the applicant to disprove the inherency. Ex parte Skinner, 2 USPQ2d 1788, 1789 (Bd. Pat. App. Int. 1986).

Here, the claims on appeal are not directed to delavirdine mesylate per se, but are limited to the S and T crystal forms of that compound. Therefore, to anticipate the claims, the prior art must disclose delavirdine mesylate in the S and T crystal forms. The examiner has provided no evidence or scientific reasoning to show that the delavirdine mesylate disclosed and claimed by Palmer is in either the S or T crystal form. Therefore, the examiner has not made out a prima facie case of anticipation by inherency.

*3 The examiner's attempt to shift the burden of proof to Appellants was premature. The burden shifts to the applicant only if the examiner can show, by evidence or scientific reasoning, a reasonable basis for concluding that the prior art product meets all the limitations of the claims. The examiner has provided no basis for such a conclusion in this case. The rejection under 35 U.S.C. § 102 is reversed.

3. Obviousness

The examiner rejected the claims under 35 U.S.C. § 103 on the basis that Palmer "discloses the free form of the instant sulfonate salts for use in treating HIV." Examiner's Answer, page 3. The examiner concluded that the corresponding methanesulfonate salt would have been an obvious variant because Palmer "teaches and in fact prefers the use of salt forms for better solubility and crystallinity," and methanesulfonate salts were exemplified for compounds other than delavirdine mesylate. Id., pages 3-4.

"In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. Only if that burden is met, does the burden of coming forward with evidence or argument shift to the applicant." In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993).

The examiner's obviousness rejection seems to suffer the same infirmity as her anticipation rejection, namely, that it is directed to delavirdine mesylate per se, rather than to the specific S and T crystal forms of delavirdine mesylate that are the subject of the claims on appeal. The examiner has provided no evidence or convincing reasoning why the prior art disclosure of delavirdine mesylate in an undefined state would have suggested the specific S and T crystal forms that are the subject of the instant claims.

Nor has the examiner established that Palmer would have enabled those skilled in the art to make the claimed S and T crystal forms of delavirdine mesylate. Appellants' specification discloses specific conditions for recrystallizing delavirdine mesylate that produce the S and T crystal forms. See pages 2-4 and Examples 1-8. Palmer does not disclose or suggest even the existence of the S and T crystal forms of delavirdine mesylate, let alone how to make them. As stated in In re Hoeksema:

> [I]f the prior art of record fails to disclose or render obvious a method for making a claimed compound, at the time the invention was made, it may not be legally concluded that the compound itself is in the possession of the public. In this context, we say that the absence of a known or obvious process for making the

claimed compounds overcomes a presumption that the compounds are obvious, based on close relationships between their structures and those of prior art compounds. *4 399 F.2d 269, 274, 158 USPQ 596, 601 (CCPA 1968) (footnote omitted).

Since the examiner has not established that Palmer would have rendered the claimed invention obvious to those skilled in the art, she has not made out a prima facie case under 35 U.S.C. § 103. The rejection for obviousness is reversed.

4. Obviousness-type double patenting

The examiner rejected the claims for obviousness-type double patenting over Palmer's claim 11. The examiner argues that the instant claims and Palmer's claim 11 are not patentably distinct because they contain "overlapping subject matter" and because Palmer also claims the free form of delavirdine, which is an obvious variant of delavirdine mesylate. Examiner's Answer, page 4.

> Obviousness-type double patenting ... requires rejection of an application claim when the claimed subject matter is not patentably distinct from the subject matter claimed in a commonly owned patent. Its purpose is to prevent an unjustified extension of the term of the right to exclude granted by a patent by allowing a second patent claiming an obvious variant of the same invention to issue to the same owner later.
> In re Berg, 140 F.3d 1428, 1431, 46 USPQ2d 1226, 1229 (Fed. Cir. 1998) (citation omitted, emphasis added).
>
> All proper double patenting rejections, of either type, rest on the fact that a patent has been issued and later issuance of a second patent will continue protection, beyond the date of expiration of the first patent, of the very same invention claimed therein (same invention type double patenting) or of a mere variation of that invention which would have been obvious to those of ordinary skill in the relevant art (obviousness-type double patenting). In the latter case, there must be some clear evidence to establish why the variation would have been obvious.
> In re Kaplan, 789 F.2d 1574, 1579-80, 229 USPQ 678, 683 (Fed. Cir. 1986) (emphasis in original).

Thus, a proper rejection for obviousness-type double patenting requires showing that the later-claimed subject matter "would have been obvious to those of ordinary skill in the relevant art" based on the claims in the earlier patent. As discussed above, the examiner has pointed to nothing in either the claims or the disclosure of the Palmer patent that would have suggested the S and T crystal forms of delavirdine mesylate to a person of ordinary skill in the art. We therefore reverse the rejection for obviousness-type double patenting.

Summary

We reverse all of the rejections because the examiner has not established that the prior art disclosed or suggested the claimed S and T crystal forms of delavirdine mesylate.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

*5 SHERMAN D. WINTERS

Administrative Patent Judge

DOUGLAS W. ROBINSON

Administrative Patent Judge

ERIC GRIMES

Administrative Patent Judge

FN1. This compound is also known as delavirdine mesylate, Appeal Brief, page 2, and we will refer to it as such.

2003 WL 21279863 (Bd.Pat.App & Interf.)

END OF DOCUMENT

2002 WL 32334598 (Bd.Pat.App & Interf.)
(Cite as: 2002 WL 32334598 (Bd.Pat.App & Interf.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)
EX PARTE PETER MEISEL, KARL-FRIEDRICH LANDGRAF, JURGEN SCHAFER, WILFRIED THIEL, MATTHIAS RISCHER, ALFRED OLBRICH, AND BERNHARD KUTSCHER
Appeal No. 2002-0438
Application No. 09/181,671
Heard: October 10, 2002

VENABLE, BAETJER, HOWARD & CIVILETTI, LLP

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WASHINGTON, DC 20005-3917

Before WINTERS, SCHEINER, and GREEN

Administrative Patent Judges

GREEN

Administrative Patent Judge

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-3 and 16. Claim 1 is drawn to Modification A of the compound 2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene, wherein the modification is "characterized by the X-ray diffractogram, reflections not coinciding with the reflections of the other two modifications being observed, inter alia, at 6.97° 2<<THETA>> (12.67 Å), 18.02° 2<<THETA>> (4.92 Å) and 19.94° 2<<THETA>> (4.45 Å)." Claims 2 and 3 are drawn to Modification B and Modification C of the 2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene compound, each modification being defined by peaks appearing on the X-ray diffractogram. Claim 16 is drawn to pharmaceuticals "comprising the modification A, B or C" of the compound, "and, if appropriate, exipients and or auxiliaries." [FN1]

The examiner relies upon the following art:

German Patent Application
Dieter et al. (Dieter) DE 42 00 259 Jul. 15, 1993

Kirk-Othmer, "Crystallization," Encyclopedia of Chemical Technology, 4th Ed., Vol. 7, pp.700-702 (1993)

The claims stand rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Dieter and Kirk-Othmer. After careful consideration of the record and the issue before us, we reverse.

DISCUSSION

The Examiner's Answer rejects claims 1-3 and 16 as being obvious over the combination of Dieter and Kirk-Othmer. Dieter is cited for teaching the compound 2-amino-4-(4-fluorobenzylamino)-1-ethoxy-carbonylaminobenzene, as well as its use in pharmaceutical compositions. Dieter does not discuss any possible crystal polymorphism of the disclosed compound.

Kirk-Othmer is cited for teaching that

> polymorphism is a condition in which a specific chemical compound may crystallize in different forms, that is, different space groups and with different physical and physico-chemical properties. An example is given of a simple compound, ammonium nitrate, with four form changes. In the paragraph which follows, it is stated that a specific **polymorph** may be absolutely essential for a particular crystalline product. By way of example, it is generally stated that one **polymorph** may have more desirable physico-chemical properties, i.e.[,] color, hardness, solubility or stability than another.
> ***2** Examiner's Answer, page 3.

The examiner notes that the instant claims are distinguishable over the prior art on the basis that it crystallized in three distinct crystalline forms, but states that "this does not render the compound in these crystalline forms patentable over the compound itself. The compound is neither new or novel, nor is its claimed use." Id. at 4. The rejection concludes that:

> It would have been obvious to one of ordinary skill in the art at the time of the invention that the three crystalline forms claimed by appellant[s] were intrinsic to the compound of the prior art, motivated by the fact that it is well known in the chemical arts that crystal polymorphism is a common and commonly recognized property of crystalline compounds.
> Id.

Appellants argue that the examiner has failed to set forth a prima facie case of obviousness. Specifically, appellants argue that, at best, the combination teaches that the claimed compound may have polymorphisms that may be separable, thus the rejection fails to provide a reasonable expectation of success in arriving at the claimed invention. See Appeal Brief, page 6. We agree.

The burden is on the examiner to make a prima facie case of obviousness, and the examiner may meet this burden by demonstrating that the prior art would lead the ordinary artisan to combine the relevant teachings of the references to arrive at the claimed invention. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). The findings of fact underlying the obviousness rejection, as well as the conclusions of law, must be made in accordance with the Administrative Procedure Act, 5 U.S.C. § 706 (A), (E) (1994). See Zurko v. Dickinson, 527 U.S. 150, 158, 119 S.Ct. 1816, 1821, 50 USPQ2d 1930, 1934 (1999). Findings of fact underlying the obviousness rejection, upon review by the Court of Appeals for the Federal Circuit, must be supported by substantial evidence within the record. See In re Gartside, 203 F.3d 1305, 1315, 53 USPQ2d 1769, 1775 (Fed. Cir. 2000). In addition, in order for meaningful appellate review to occur, the examiner must present a full and reasoned explanation of the rejection. See, e.g., In re Lee, 277 F.3d 1338, 1342, 61 USPQ2d 1430, 1432 (Fed. Cir. 2002).

The rejection of record does not meet the above criteria. Dieter, while teaching the compound that is the subject of the claims is known, does not teach or suggest that the compound has different crystalline structures. Thus, the rejection of record does not set forth any motivation to combine Dieter with Kirk-Othmer

because, although Kirk-Othmer does teach that it is known that crystal polymorphism is known generally to exist, there is no teaching or suggestion in the references that the compound of the claimed invention is known to exhibit such polymorphism.

*3 Moreover, the record demonstrates that the compound as prepared by the prior art is a mixture of crystal **polymorphs**, whereas appellants have succeeded in isolating thee distinct **polymorphs**, i.e., Modifications A, B and C. See Declaration of Wilfried Thiel, Paper No. 9. Thus, the isolated crystal **polymorphs** as claimed in the instant application do not appear to be an inherent property of the claimed compound as disclosed by the prior art of record.

CONCLUSION

Because the rejection of record does not set forth a prima facie case of obviousness, it is reversed.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

Sherman D. Winters

Administrative Patent Judge

Toni R. Scheiner

Administrative Patent Judge

Lora M. Green

Administrative Patent Judge

FN1. Note that the panel is interpreting this claim as requiring one of Modification A, Modification B or Modification C, but excluding mixtures of the disclosed modifications.

2002 WL 32334598 (Bd.Pat.App & Interf.)

END OF DOCUMENT

2003 WL 22282265 (Trademark Tr. & App. Bd.)
(Cite as: 2003 WL 22282265 (Trademark Tr. & App. Bd.))

*1 THIS OPINION WAS NOT WRITTEN FOR PUBLICATION

Board of Patent Appeals and Interferences

Patent and Trademark Office (P.T.O.)
EX PARTE RICHARD P. POLNIASZEK, XUEBAO WANG, JEFFREY S. DEPUE, CHENNAGIRI R. PANDIT, YADAGIRI PENDRI, AND EDUARDO J. MARTINEZ
Appeal No. 2001-1805
Application No. 09/141,402

NO DATE REFERENCE AVAILABLE FOR THIS DOCUMENT

MARLA J MATHIAS

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Before WINTERS, SCHEINER, and ADAMS

Administrative Patent Judges

ADAMS

Administrative Patent Judge

ON BRIEF

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 41, which is the only claim pending in the application and is reproduced below:

41. A high melt **polymorph** of the compound N-(3,4-dimethyl-5-isoxazolyl)-4'- (2-oxazolyl)[1,1'-biphenyl]-2-sulfonamide, which has a melting point of approximately 143.07 to 145.1° C.

The examiner relies on:

Murugesan 5,612,359 Mar. 18, 1997

GROUND OF REJECTION

Claim 41 stands rejected under 35 U.S.C. § 103 as obvious over Murugesan.

DISCUSSION

At the outset, we wish to make it clear that "reliance on per se rules of obviousness is legally incorrect" and must stop. In re Ochiai, 71 F.3d 1565, 1572, 37 USPQ2d 1127, 1133 (Fed. Cir. 1995). Accord, In re Brouwer, 77 F.3d 422, 425, 37 USPQ2d 1663, 1666 (Fed. Cir. 1996).

A per se approach would be in conflict with long standing precedent as to the relevance of the method of making a product to the obviousness of the product. Note In re Payne, ("[a]n invention is not 'possessed' absent some known or obvious way to make it.") citing In re Hoeksema, 399 F.2d 269, 274, 158 USPQ 596, 601 (CCPA 1968). In a similar manner, the court in In re O'Farrell, 853 F.2d 902, 7 USPQ2d 1673, 1680 (Fed. Cir. 1988), in considering the Polisky reference relative to the rejected claims stated "Polisky contained detailed enabling methodology for practicing the claimed invention, a suggestion to modify the prior art to practice the claimed invention, and evidence suggesting that it would be successful." (Emphasis added). See also, In re Lalu, 747 F.2d 703, 705, 223 USPQ 1257, 1258 (Fed. Cir. 1984) ("[t]he prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compounds.")

***2** Since there are no per se rules of obviousness or nonobviousness, each case must be decided upon the facts in evidence in that case. See In re Cofer, 354 F.2d 664, 667, 148 USPQ 268, 271 (CCPA 1966) ("[n]ecessarily it is facts appearing in the record, rather than prior decisions in and of themselves, which must support the legal conclusion of obviousness under 35 U.S.C. § 103"); and Ex parte Goldgaber, 41 USPQ2d 1172, 1176 (Bd. Pat. App. & Int. 1995) ("each case under 35 U.S.C. § 103 is decided on its own particular facts.").

We find the examiner's argument (Answer, page 4), "[t]he Court [in] In re Cofer expands upon rather than rejects what the Appellants term a 'purported [per se] rule"' legally flawed and in error. As set forth supra, our appellate reviewing court has made it clear that there are no per se rules of obviousness.

As a second error, we find that the examiner failed to provide any rationale or analysis to support her position in either the Answer or the Final Rejection. For emphasis we reproduce in full the examiner's statement of the rejection from page 3 of the Answer -- "Claim 41 is rejected under 35 U.S.C. [§] 103(a) as being unpatentable over ... Murugesan." In this regard, we suggest the examiner review the Manual of Patent Examining Practice (MPEP) § 706.02(j) for a model of how to explain a rejection under this section of the statute. Furthermore, we direct the examiner's attention to MPEP § 1208, "[a]n examiner's answer should not refer, either directly or indirectly, to more than one prior Office action." In this instance the Answer neither provides a reasoned explanation of the rejection, nor does it direct our attention to any prior Office action where a reasoned analysis of the facts is provided.

Contrary to the examiner's position (Answer page 5) [FN1], we find the N-(3,4-Dimethyl-5-isoxazolyl)-4'-(2-oxazolyl)[1,1'-biphenyl]-2-sulfonamide compound set forth in Example 1(D) of Murugesan to be the most relevant compound to appellants' claimed invention. However, as appellants point out (Brief, page 4) Murugesan "discloses an amorphous form of this compound, having a melting point of 90 to 98° C....." Stated differently, notwithstanding that the claimed compound has the same formula as Murugesan, the examiner has not established that Murugesan suggests appellants' specifically claimed **polymorph**. This is clearly demonstrated by the different melting points for the two compounds.

We note the examiner's analysis of the N-(3,4-Dimethyl-5-isoxazolyl)-4'-(5-

oxazolyl)[1,1'-biphenyl]-2-Sulfonamide compound set forth in Murugensan's example 4, wherein she states (Answer, page 6) that a "difference in bonding location would result, as expected in any isomeric situation, in certain differences in physical properties. Here, one such difference is reflected in melting points that range from 189-191° C[] for the Murugesan compound compared to 143-145° C[] for the instantly claimed compound." However, the problem with this argument should be self evident (Answer, page 6), the "compound taught by Murugesan differs from the instantly claimed compound ... at the 5-oxazolyl position...." As appellants argue (Reply Brief, page 2), "[w]hile Example 4 of ... [Murugesan] indeed discloses a crystalline form of a compound having a melting point of 189-191° C, it fails to disclose or suggest the invention of claim 41 ... having a melting point of approximately 143-145° C." Stated another way, they are different compounds.

*3 The claimed invention is drawn to a specific polymorphic form of N-(3,4-Dimethyl-5-isoxazolyl)-4'-(2-oxazolyl)[1,1'-biphenyl]-2-sulfonamide that has a melting point of approximately 143-145° C. The prior art relied upon by the examiner does not teach this specific **polymorph** as claimed by appellants. The examiner failed to demonstrate that the prior art even recognized that the claimed compound exists in different polymorphic forms, or that there is a known or obvious way to manufacture the specific polymorphic form claimed. Hoeksema. Stated differently, the examiner failed to demonstrate that Murugesan provides an enabling disclosure of the compound set forth in appellants' claim 41. In contrast the examiner has not rejected appellants' claims under 35 U.S.C. § 112, first paragraph, thus the examiner has found on this record that appellants' specification provides an enabling disclosure of how to make and use the claimed invention.

For the foregoing reasons we reverse the rejection of claim 41 under 35 U.S.C. § 103 over Murugesan.

REVERSED

BOARD OF PATENT APPEALS AND INTERFERENCES

Sherman D. Winters

Administrative Patent Judge

Toni R. Scheiner

Administrative Patent Judge

Donald E. Adams

Administrative Patent Judge

FN1. At page 5 of the Answer, the examiner finds that "[e]xample 4 of Murugesan is believed to be the most relevant and most critical to the issue of obviousness for the instant application.".